42* Do false positive test results for newborn screening for cystic fibrosis lead to long term parental anxiety?

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Objective: to evaluate whether parental anxiety induced by a false positive screening test result disappears after six months and to assess whether a special program to inform the parents prior and during the screening procedure prevents or diminishes parental anxiety.
Study design: Prospective controlled study assessing the long term effects of false-positive test results of newborn screening for CF on parental anxiety and stress by means of questionnaires sent to parents of 106 infants with a false positive newborn screening test and of 318 randomly selected infants with a true negative screening test. Semi-structured in-depth interviews with 25 parents of the false-positive group.
Results: Parents showed negative feelings after being informed about the positive screening test result which increased significantly with the time gap between the news of the test result and the follow-up test. After confirmation their child was healthy and not suffering from CF, they felt reassured in most cases. After six months no difference in anxiety levels between both groups of parents was found. Well-informed parents in the false positive group experienced less stress than less well informed parents. Parents opinion of their infant's health was not different between the false-positive and control group.
Conclusions: Initial anxiety after a positive screening test result increases strongly with a delay in the follow-up procedure, but false positive test results for newborn screening for CF do not seem to cause long-term parental anxiety. Well-informed parents showed lower stress levels.

43 Atypical forms of cystic fibrosis (CF): The emerging diagnostic challenge for diagnosing CF in children and adolescents with a single-organ involvement

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Objectives: Patients with a non-classic form of Cystic Fibrosis (CF) may present a single organ involvement. They have non-diagnostic sweat chloride test values and/or they are carrier of two not clearly demonstrated CF-causing mutations. The aim of our study was to identify atypical forms of CF in a pediatric population affected by recurrent pancreatitis.
Methods: We enrolled 105 consecutive young patients (53 M, mean age at diagnosis 8.9±5.4 yrs, range 4 months – 18 yrs) affected by recurrent pancreatitis of several etiologies. All patients were tested for CF by a sweat chloride test and a CFTR gene sequencing was done for most of them. A pathological sweat test revealed classic CF at its onset in two patients. Border-line sweat chloride values were found in 8 (7.6%) patients. We detected CFTR gene mutations in 35.5% (22/62) of patients. Only two patients with border-line sweat chloride values had two CFTR gene mutations (1 surely CF-causing); one of them was diagnosed as having classic CF when he developed bronchiectasis during clinical follow-up.
Conclusions: We observed a high percentage of patients (7.6%) with borderline sweat chloride values. Only two of these patients had 2 FTR gene mutations (but only one known CF-causing mutation); clinical follow-up was determinant for diagnosing CF in one of them. We also identified 8 patients carrying two CFTR gene mutations but they had a negative sweat test. These patient groups currently represent a challenge for a correct CF diagnosis. In the absence of sure diagnostic investigations, only clinical features and follow-up may lead clinicians to confirm or, ultimately, to exclude CF.

44* Difficult counseling situations – lessons from a cystic fibrosis expertise laboratory

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Cystic Fibrosis is the most common autosomal recessive disorder. The carrier frequency in Greece is estimated at 5% of general population. The Department of Medical Genetics, University of Athens has been offering molecular analysis of the CFTR gene since 1992. During that time we have screened more than 10.500 members of the general population, 700 patients of Greek origin and done more than 500 prenatal diagnoses.
Due to the great molecular heterogeneity of the Greek population, the four most common mutations [p.F508del (54.6%), c.621+1G>T (6.22%), p.G542X (3.66%) and p.N1303K (2.39%)] cover only 66.9% of the mutations found. That signifies that a large number of CF causing alleles are found rarely or even in single families. The low incidence of these rare mutations as well as novel mutations which can be only be assessed through *in-silico* analysis, pose a problem in genetic counseling. Can we safely assign a "carrier status" or inform for the outcome of a pregnancy when the couple carries such mutations?
In our laboratory we have also been facing dilemmas in cases where known and functionally assessed disease causing mutations, have been found in homozygosity in healthy individuals, disease causing mutations have been found in compound heterozygotes with no CF phenotypic features and in cases where we have to counsel couples carrying a novel and a disease causing mutation.
We will be presenting these special cases and discussing the difficulties in genetic counseling.

45* Meconium ileus in cystic fibrosis newborn screening (CF NBS)

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Objectives: Comparison between patients with Meconium ileus (MI) and without MI (non-MI) diagnosed in CF NBS.
Methods: Groups of MI and non-MI patients diagnosed in CF NBS with the same age, gender and CFTR mutations were analyzed. Birth weight, age at diagnosis, IRT, sweat test values and evaluation of nutritional status in the 1st year of life were collected.
Results: From Sept. 2006 to the end of August 2010 there were 430 979 newborns screened. CF was confirmed in 80 cases. 13 patients with MI and 13 non-MI were analyzed. Both groups consisted of 6 F508del homozygotes; 5 F508del hetertozygotes and 2 non-F508del heterozygotes. All patients were pancreatic insufficient. Average age at diagnosis in MI group was similar to non-MI patients (c. 6 weeks). The mean birth weight and average sweat test values showed no significant differences between the groups. The mean IRT for the group MI (410.54±363.35) was significantly lower than in the non-MI patients (749.15±367.46) ($p = 0.0266$). Average SDS body weight (–1.18±0.81v 0.04±0.81; $p = 0.0008$) and SDS height (–1.18±0.81 v 0.04±0.81; $p = 0.0008$) in the 1st year of life were considerably reduced in MI patients. Thus, IWH% in MI patients (90.38±8.4) was lower than for the non-MI group (103.15±11.22) $p = 0.0031$.
Conclusion:

1. Lower (nearer to normal) IRT values in MI patients might lead to diagnostic difficulties. Neonatal teams should mark the importance of reporting MI cases to the Screening Centre.
2. Worse somatic development of MI patients after the 1st year of life, despite early diagnosis, underlines the importance of intensive nutritional monitoring and treatment of CF patients with MI.